

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
25 November 2004 (25.11.2004)

PCT

(10) International Publication Number
WO 2004/100773 A3

(51) International Patent Classification⁷: **C07H 21/02, 21/04, A01N 63/00, 65/00, C12N 5/00, 5/02, A01K 67/00, 67/033**

(74) Agent: **LOCKHART, Helen, C.; Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA 02210 (US).**

(21) International Application Number:
PCT/US2004/014996

(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: **12 May 2004 (12.05.2004)**

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(25) Filing Language: **English**

Published:

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(26) Publication Language: **English**

(88) Date of publication of the international search report:
3 February 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(30) Priority Data:
60/470,046 13 May 2003 (13.05.2003) US

(71) Applicant (*for all designated States except US*): **THE REGENTS OF THE UNIVERSITY OF COLORADO [US/US]; 4001 Discovery Drive, Suite 390, Campus Box 588, Boulder, CO 80309 (US).**

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **NEWELL ROGERS, Martha, Karen [US/US]; 3930 Mariposa Street, Colorado Springs, CO 80907 (US). VILLALOBOS-MENUET, Elizabeth [US/US]; Biology Department, University of Colorado - Colorado Springs, 1420 Austin Bluffs Parkway, SB266, Colorado Springs, CO 80918 (US). MELAMEDE, Robert [US/US]; Biology Department, University of Colorado - Colorado Springs, 1420 Austin Bluffs Parkway, SB266, Colorado Springs, CO 80918 (US). CAMLEY, Robert [US/US]; Biology Department, University of Colorado - Colorado Springs, 1420 Austin Bluffs Parkway, SB266, Colorado Springs, CO 80918 (US).**

WO 2004/100773 A3

(54) Title: **DIAGNOSTIC AND THERAPEUTIC TREATMENTS RELATED TO MITOCHONDRIAL DISORDERS**

(57) Abstract: The invention is based in part on the discovery that chromosomal disorders such as Down Syndrome can be diagnosed by assessing maternal mitochondrial status. Thus the invention relates to diagnostic and therapeutic methods and related products for chromosomal disorders such as Downs Syndrome, for example, for identifying a risk of fetal Downs syndrome and methods of mitigating that risk. The methods also re useful for other therapies where it is desirable to manipulate mitochondria such as tissue generation.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/14996

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/02,21/04; A01N 63/00, 65/00; C12N 5/00, 5/02; A01K 67/00,67/033
 US CL : 536/23.1; 424/93.1; 435/325; 800/8

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 424/93.1; 435/325; 800/8

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
 EAST, STN, PubMed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	(ANONYMOUS) "MitoTracker and MitoFluor Mitochondrion-Selective Probes". In: Molecular Probes Product Information. December 2002, page 1, column 1, lines 9-11.	9, 30
A	BUSCIGLIO, J et al. Altered Metabolism of the Amyloid β -Precursor Protein Is Associated with Mitochondrial Dysfunction in Down's Syndrome. <i>Neuron</i> . 28 February 2002, Vol. 33, pages 677-688, especially page 677.	12
A	JEZEK, P. Possible physiological roles of mitochondrial uncoupling proteins—UCPn. <i>International Journal of Biochemistry & Cell Biology</i> . 2002, Vol. 34, pages 1190-1206.	11, 31-36
X	ARBUZOVA et al. Mitochondrial dysfunction and Down's syndrome. <i>Bioessays</i> . 2002, Vol. 24, pages 681-684.	1-12, 22-30

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

29 October 2004 (29.10.2004)

Date of mailing of the international search report

01 DEC 2004

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
 Commissioner for Patents
 P.O. Box 1450
 Alexandria, Virginia 22313-1450

Faxsimile No. (703) 305-3230

Authorized officer

Joanne Hama, Ph.D.

Telephone No. (571) 272-2911